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Sequelae of COVID-19 in Hospitalized Children: A 4-Months Follow-Up

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Abstract: Little is known about the sequelae of SARS-CoV-2 infection in children. In a COVID-19 dedicated clinic, we followed-up for 4 months 25 children previously hospitalized for COVID-19, performing clinical, laboratory, and lung ultrasound evaluation. Mid-term sequelae were rarely observed in our COVID-19 children's cohort.

Key Words: SARS-CoV-2, COVID-19, lung ultrasound, follow-up, children
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Since the beginning of the novel coronavirus pandemic, children have been less frequently and severely involved than adults, requiring hospitalization only in 5%–10% of cases.[1]

During the pandemic peak in Italy, public health services were overwhelmed, and little is known about the follow-up of children that required hospital care for SARS-CoV-2 infection. In Piedmont, home checks of discharged children were often limited to the nasal swab testing, without a proper medical evaluation. For this reason, we organized a clinic in the Regina Margherita Children's Hospital, in Turin, exclusively dedicated to the postdischarge follow-up of COVID-19 affected children. Two weeks after the discharge, we performed an initial evaluation by phone, followed by an assessment in the ambulatory clinic. A separate entrance was provided away from the other patients for our COVID-19 clinic and a dedicated nurse and pediatrician fully equipped with all the necessary personal protective equipment. Blood analysis, nasal swab, lung ultrasound, and medical evaluation were carried out for each patient. Moreover, a by-phone follow-up is currently ongoing, accounting for, on average, 130 days from the discharge [interquartile range: 106–148 days].

Among 28 patients admitted to the pediatric COVID-department, from March 1 to June 1, 2020, 25 (89%) accepted coming back for the medical evaluation, which was performed on average 35 days postdischarge (interquartile range: 19–46 days). Epidemiologic, clinical, and laboratory features of the patients are summarized in Table 1. Of the 25 children enrolled, 13 were male and 12 female, with a median age of 7.75 years (range 0.4–15 years). A respiratory form of SARS-CoV-2 infections affected all of them and there were no cases of COVID-19-related multisystem inflammatory syndrome. Regarding comorbidities, one patient is affected by cystic fibrosis, and one had congenital heart disease. According to the definitions provided by Qiu,[2] 7 (28%) of them were previously admitted for a mild COVID-19, 14 (56%) for moderate disease, and 4 (16%) showed a severe form of COVID-19. At hospital admission, 13 (52%) patients had a pathologic lung ultrasound (62% of them showed a diffuse interstitial pattern, and 38% had both subpleural multiple consolidations and diffuse interstitial pattern). As previously observed,[3] lung ultrasound improved concomitantly with the patient's clinical condition. Nevertheless, at the follow-up examination, we still observed a mild interstitial pattern in 3 patients and multiple subpleural consolidations in other 2 cases. One of them was investigated again a month later, with a complete lung ultrasound normalization; the other one, affected by cystic fibrosis, displayed findings probably related to their chronic lung disease.

All patients had a normal hemoglobin value, lymphocyte count, and C-reactive protein at the follow-up check, but in 5 patients, we found persistence of altered inflammatory markers (ferritin, fibrinogen, or D-dimer). At a second examination, 6 weeks postdischarge, all those 5 children showed normal blood analysis.

We investigated the presence of IgG directed toward SARS-CoV-2 using ELISA assay (In3diagnostic Eradikit COVID-19, Turin, Italy, reported sensibility for IgG: 96%) in 24 on 25 patients: 20 (83%) children had detectable levels of SARS-CoV-2-specific IgG, 4

TABLE 1. Epidemiologic, Laboratory, and Clinical Features of COVID-19 Pediatric Patients at Hospital Admission and Follow-up Visit

	Hospital Admission	Ambulatory Follow-up
Epidemiologic data		
Female patients	13	
Male patients	12	
Age, yr (SD, range)	7.75 (0.4–15)	
Family members with COVID-19	24/25	
Laboratory tests (references values—alteration)		
White blood cells—(reference values according to the age)—decreased	2/22	0/25
Lymphocytes—(reference values according to the age)—decreased	4/22	0/25
Platelets—(150,000–450,000/mmc)—decreased	6/22	0/25
C-reactive protein—(<5 mg/L)—increased	3/22	0/25
D-dimer—(<500 ng/mL)—increased	11/16	1/25
Erythrocyte sedimentation rate—(3–13 mm/h)—increased	8/11	2/25
Fibrinogen—(200–400 mg/dL)—increased	5/16	1/25
Ferritin—(12–60 (ng/mL)—increased	7/14	3/25
Alanine aminotransferase—(8–40 UI/L)—increased	3/21	0/25
Creatinine—(reference values according to the age)—increased	2/21	1/25
SARS-CoV-2 test		
SARS-CoV-2 *pcr* detection on nasal swab	25/25	0/25
SARS-CoV-2-specific IgG positivity	N/A	20/24
Pathologic lung ultrasound	13/24	5/25
Pulmonary consolidation	5	2
Interstitial B-lines pattern	13	5

(17%), despite a positive nasal swab at admission, showed a negative serology. Furthermore, we screened the persistence of positive nasal swab in our cohort: 9 (36%) children were discharged (with a still positive nasal swab with the recommendation to home quarantine), while, at the follow-up, all nasal swabs were negative.

An underestimated aspect of the follow-up of COVID-19 affected children is the fear of resulting positive again after one or more negative swab results. In our experience, 3 families (10.7%) refused to participate at the postdischarge program due to the anxiety about being found still positive for SARS-CoV-2 and to be forced to additional 14–21 days of mandatory home isolation. Psychologic obstacles in the families of COVID-19 children are described[4] and must be taken into consideration for the correct management of these patients.

In conclusion, a month after the discharge, all nasal swabs became negative, suggesting the complete clearance of the virus in those more severe pediatric patients who required hospitalization. Second, lung ultrasound findings correlated with the clinical improvement, showing a complete normalization within 5 weeks from hospital discharge in the majority of patients. Eventually, all our patients showed a clinical and complete laboratory recovery about a month after discharge, without manifestation of any COVID-19-related sequelae 4 months later. An extended time follow-up is necessary to describe better the natural history of COVID-19 in children in the long-term period, but the rarity of mid-term sequelae allows us to predict a good prognosis of SARS-CoV-2 infection in the pediatric age.

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COVID-19 Gastrointestinal Manifestations Are Independent Predictors of PICU Admission in Hospitalized Pediatric Patients

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Abstract: Multicenter study conducted in 15 hospitals including 101 COVID-19 pediatric inpatients aiming to describe associated gastrointestinal (GI) manifestations. GI symptoms were present in 57% and were the first manifestation in 14%. Adjusted by confounding factors, those with GI symptoms had higher risk of pediatric intensive care unit admission. GI symptoms are predictive of severity in COVID-19 children admitted to hospitals.

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The novel coronavirus (SARS-CoV-2) outbreak started in China in December 2019. The rapid transmission of the infection and its virulence forced the World Health Organization to declare the associated disease (COVID-19) an international public health emergency.

The typical clinical picture of COVID-19 in previously healthy children is a mild or even asymptomatic disease, with practically no associated mortality. It is well known that fever and respiratory symptoms, such as dry cough or dyspnea, are the most frequently observed. However, as knowledge of COVID-19 has progressed, symptoms affecting any other organ or system have been described.[1]

Frequency of gastrointestinal (GI) symptoms, previously thought to be scarce, has increased with the progression of the pandemic. They are of special interest in the pediatric age group, especially after the first descriptions of a multisystemic inflammatory syndrome (MIS-C), resembling Kawasaki Disease, in which GI symptoms such as diarrhea, abdominal pain, or vomiting are prominent.[2]

Uncertainties about this disease are greater at the pediatric age. The objective of our study was to describe COVID-19 GI manifestations of hospitalized pediatric patients.

METHODS

Study Design

Multicenter, descriptive, observational study conducted in 15 hospitals in Spain, in COVID-19 pediatric patients admitted from March 1 to June 3, 2020.